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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/893,346	06/28/2001	Wayne D. Comper	48643-015	2638

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
01/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/893,346	COMPER, WAYNE D.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,9-14,16,17,20,23 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,9-14,16,17,20,23 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/22/07; 10/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 22, 2007 has been entered. Claims 1-5, 7, 9-14, 16, 17, 20, 23 and 25 remain pending and under examination.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7, 9-14, 16, 17, 20, 23 and 25 remain rejected under 35 U.S.C. 112, first paragraph, because the specification is only enabling for some of the claimed embodiments. The specification is enabled for a method of assessing therapeutic effectiveness of a treatment agent for renal disease and/or renal complications of a disease or condition, comprising assaying for total albumin protein content via HPLC compared with total albumin protein content via radioimmunoassay using antibodies to native albumin. The specification is not enabling for a method of assessing therapeutic effectiveness of a treatment agent for renal and/or renal complications of a disease or condition, comprising assaying for any protein (non-albumin) via the steps claimed.

The breadth of the claims encompasses the assessment of therapeutic effectiveness of a treatment agent for renal disease and/or renal complications of a disease or condition, wherein any protein can be measured in terms of total protein content (native and intact-modified). The nature of the invention is the identification of intact-modified protein present in the urine, indicative of problems with the processing of proteins through the kidneys. The state of the art demonstrates that Applicant has successfully characterized immunochemically nonreactive urinary albumin using HPLC (Osicka and Comper, *Clinical Chemistry*, 2004, 50(12):1-6, cited in the affidavit filed October 4, 2004).

The level of skill in the art is high, evidenced by the inventor and those in the field cited in the references of the information disclosure statements and the instant specification. The level of predictability in the art with regard to identifying intact-modified protein present in urine in patients with renal disease/complications is limited to identification of albumin. The specification does not provide guidance for identifying other intact-modified proteins other than albumin that are present in urine in patients with renal disease/complications. While such intact-modified albumin has been demonstrated as indicative of renal disease/complications, no other protein in humans has been identified as intact-modified *and* indicative of renal disease/complication.

Given that the disclosure only offers a hypothesis on how albumin becomes intact/modified, one would not be able to assume that that hypothesis relates to globulin or any other protein until a mechanism is understood. While a mechanism is not required to practice the invention with albumin being the monitored protein, extrapolating data from albumin to other

proteins without understanding the mechanism or doing any experimentation on other proteins is not reliable.

With regard to the identification of intact-modified proteins via HPLC, it is understood that once the intact-modified proteins from the patient are identified via HPLC, one would be able to make antibodies that specifically bind to those intact-modified proteins. However, one would expect that the intact-modified proteins would be patient-specific and not useful for detecting intact-modified protein from a different patient. Therefore, the initial step in detecting total protein content must include a step of HPLC, since known antibodies to native albumin have been shown to be non-reactive with intact-modified urinary albumin.

Given the breadth of the claims, the nature of the invention, the high level of skill in the art, the state of the art, the low level of predictability, the limited guidance and examples in the specification relating to intact-modified albumin, the full scope of the claims is not enabled.

Response to Arguments

3. Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that the presence of any protein, not just albumin, is indicative of renal failure. Applicant points to the declaration of Dr. Comper, filed September 11, 2002 (though previously indicated by the Office and Applicant as filed on August 15, 2003) previously filed, entered, and addressed by the Office, all of record. The declaration shows that intact modified proteins such as IgG and transferrin were detected in diabetic rat urine. Applicant also points to an article published by the

National Kidney Foundation, which shows that diabetes results in injury to the small blood vessels of the kidneys, resulting in increased protein in the urine. Applicant argues that the methods of the present invention provide urinary protein profiles that are significantly different from those obtained using conventional methods for measuring protein (immunoassay). Applicant argues that these methods are applicable to any protein detectable in the urine, not just albumin.

- In response to Applicant's arguments, the Office acknowledges that kidney failure results in increased protein in the urine. The Office also acknowledges that not only albumin protein would be detected in the urine, but other proteins would also be present in the urine in increasing amounts. This is evidenced by the article referenced by Applicant published by the National Kidney Foundation. The Office does not dispute that renal failure results in increased protein in the urine.
- The Office maintains its position that it is critical to obtain total protein content using HPLC, since Applicant has not identified any antibodies that are capable of binding to the intact modified proteins as claimed. Given Applicant's disclosure, it is understood that total protein content could theoretically be determined using antibodies that bind to intact modified protein; however, this cannot take place until the intact modified protein is identified by HPLC. For Applicant to rely on first detecting intact modified protein by HPLC, then engineering antibodies that bind to that specific intact modified protein, and then applying the antibodies to a method as instantly described is not reflected in the claims. The claim language

of the methods does not indicate that HPLC is required for identifying intact modified protein.

- Applicant also argues that there is no evidence of patient-specific protein modification, as alleged by the examiner, and that proteins are modified on the basis of their structure.
  - In response to Applicant's argument, the protein modifications through the kidneys that result in intact modified protein are not uniform modifications. Applicant does not even know exactly how the modifications take place and have only hypothesized that different epitopes on the proteins are revealed due to processing through a compromised kidney. In the case of intact modified albumin, Applicant has not identified a single epitope that is common to intact modified albumin obtained from multiple patients. Even if Applicant's hypothesis is later confirmed, one would reasonably expect that the modifications of the proteins processed by failing kidneys would differ from patient to patient given the degree of renal failure.

Conclusion

4. No claim is allowed. All claims are drawn identical subject matter that was rejected in the Office action of July 20, 2007. Applicant's arguments and the Office's responses to those arguments are virtually identical. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30), alternate Fridays off,. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 1-2-2008
Primary Examiner, TC1600